

Indomethacin-based PROTACs as pan-coronavirus antiviral agents

Jenny Desantis,^{a,1} Beatrice Mercorelli,^{a,1} Marta Celegato,^a Federico Croci,^b Alessandro Bazzacco,^a

Massimo Baroni,^c Lydia Siragusa,^d Gabriele Cruciani,^b Arianna Loreanian,^{a,2,§} Laura Goracci^{b,2,§}

¹ co-first authors

² co-last authors

[§] corresponding authors: laura.goracci@unipg.it; arianna.loregian@unipd.it

Affiliations

^a Department of Molecular Medicine, University of Padua, Padua, Italy.

^b Department of Chemistry, Biology, and Biotechnology, University of Perugia, Italy

^c Molecular Discovery Ltd., Centennial Park, Borehamwood, Hertfordshire, United Kingdom

^d Molecular Horizon, srl, Bettona 06084, Italy

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Table S1: NMR Chemical Shifts

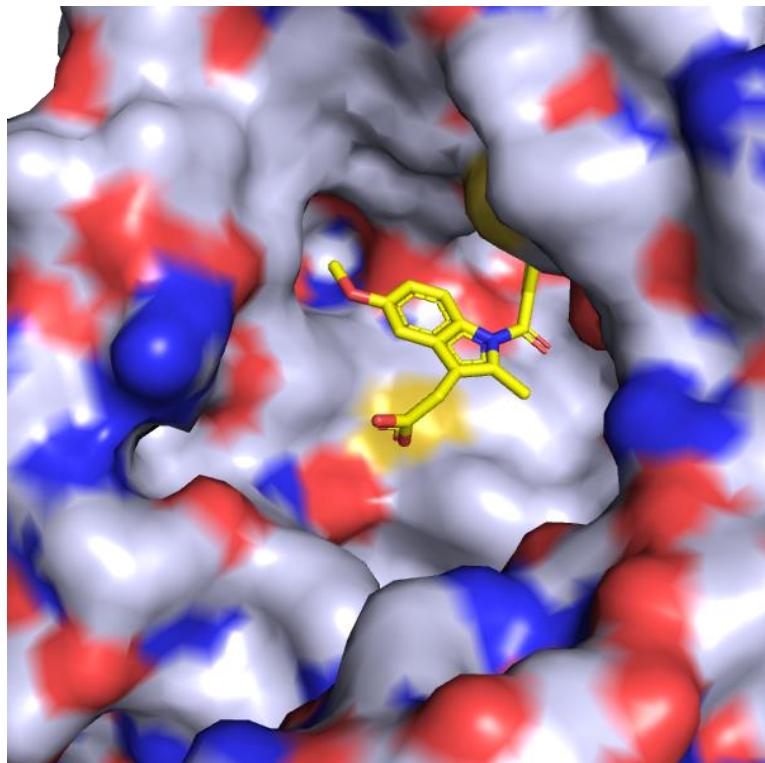


Figure S1: INM in mPGES-2 according to the PDB ID 1Z9H x-ray structure.

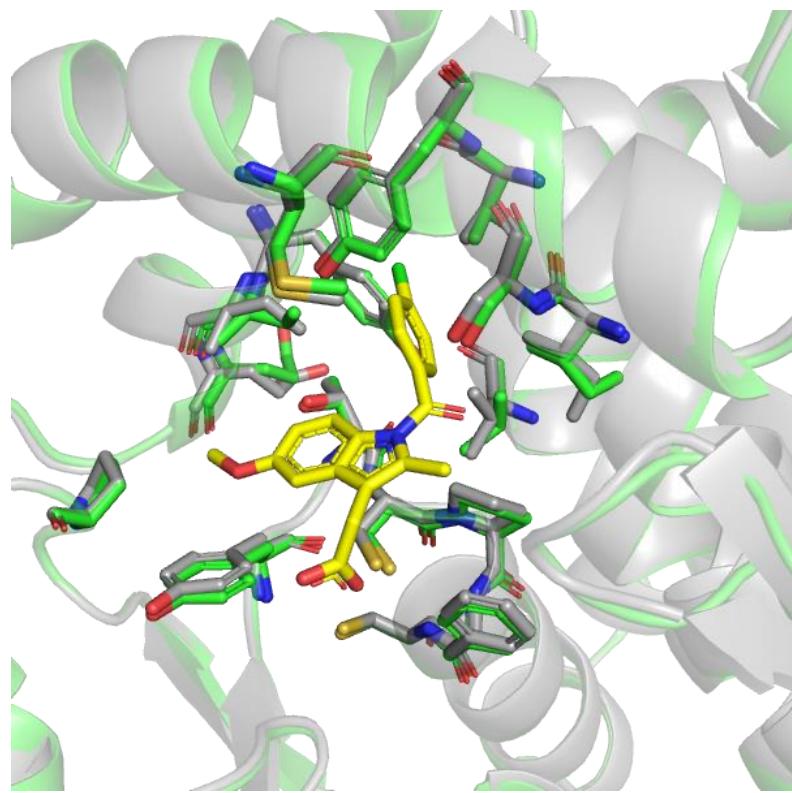
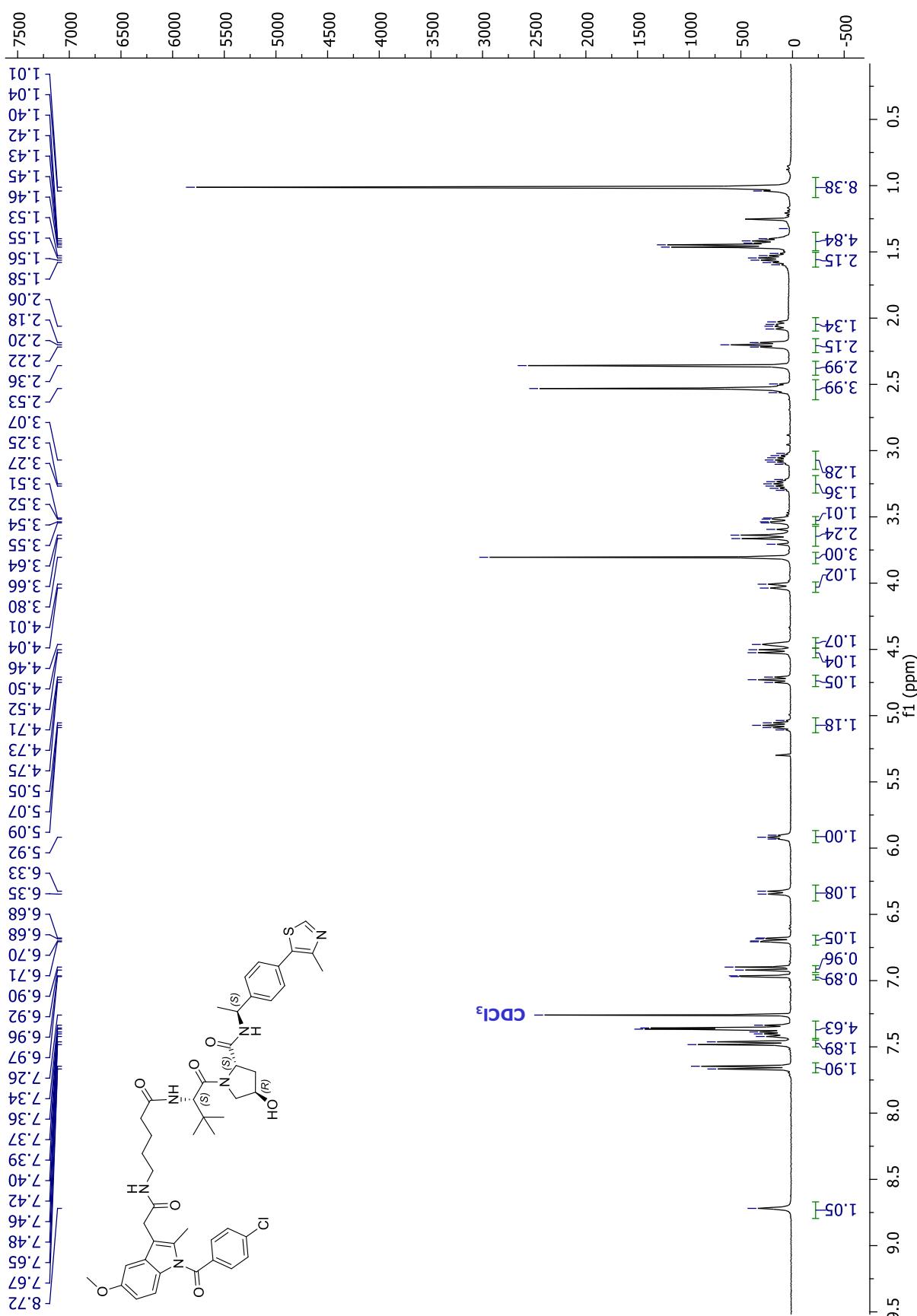


Figure S2: Overlap of PDB ID 1Z9H (x-ray structure from *Macaca fascicularis*, co-crystallized with INM) and the homology model for human mPGES2.



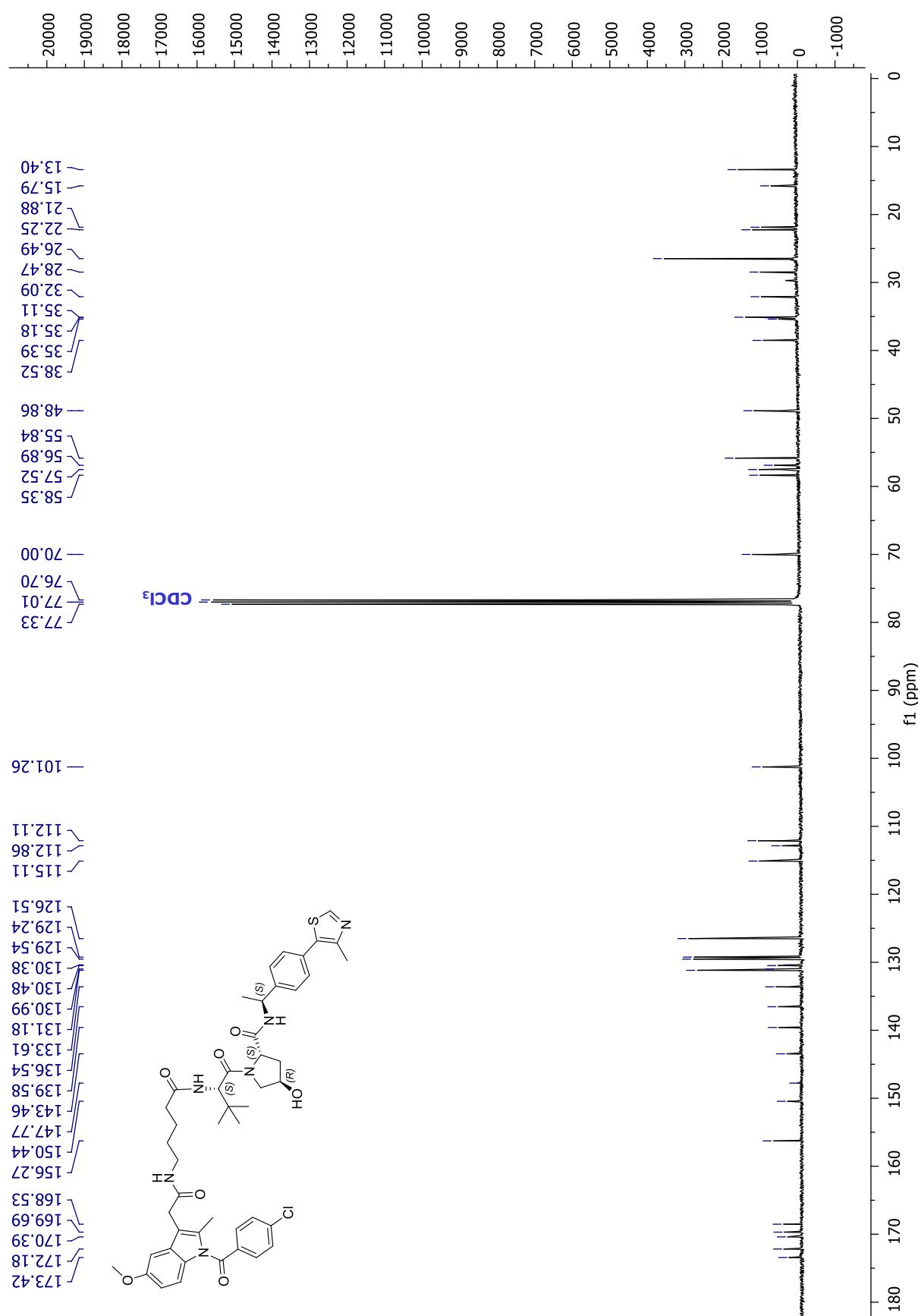


Figure S4. ^{13}C NMR (101 MHz, CDCl₃) spectrum of compound 2.

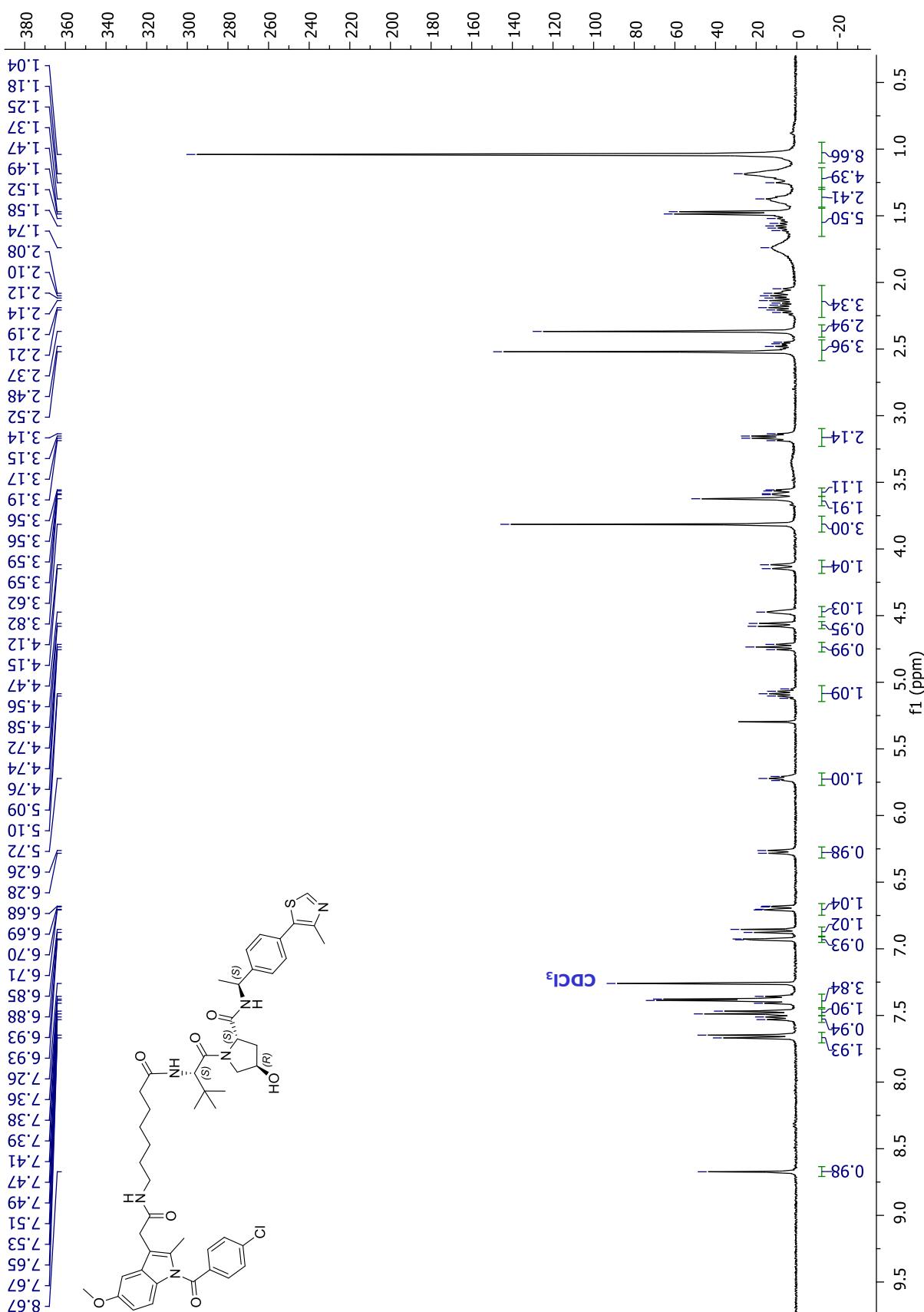


Figure S5. ^1H NMR (400 MHz, CDCl_3) spectrum of compound 3.

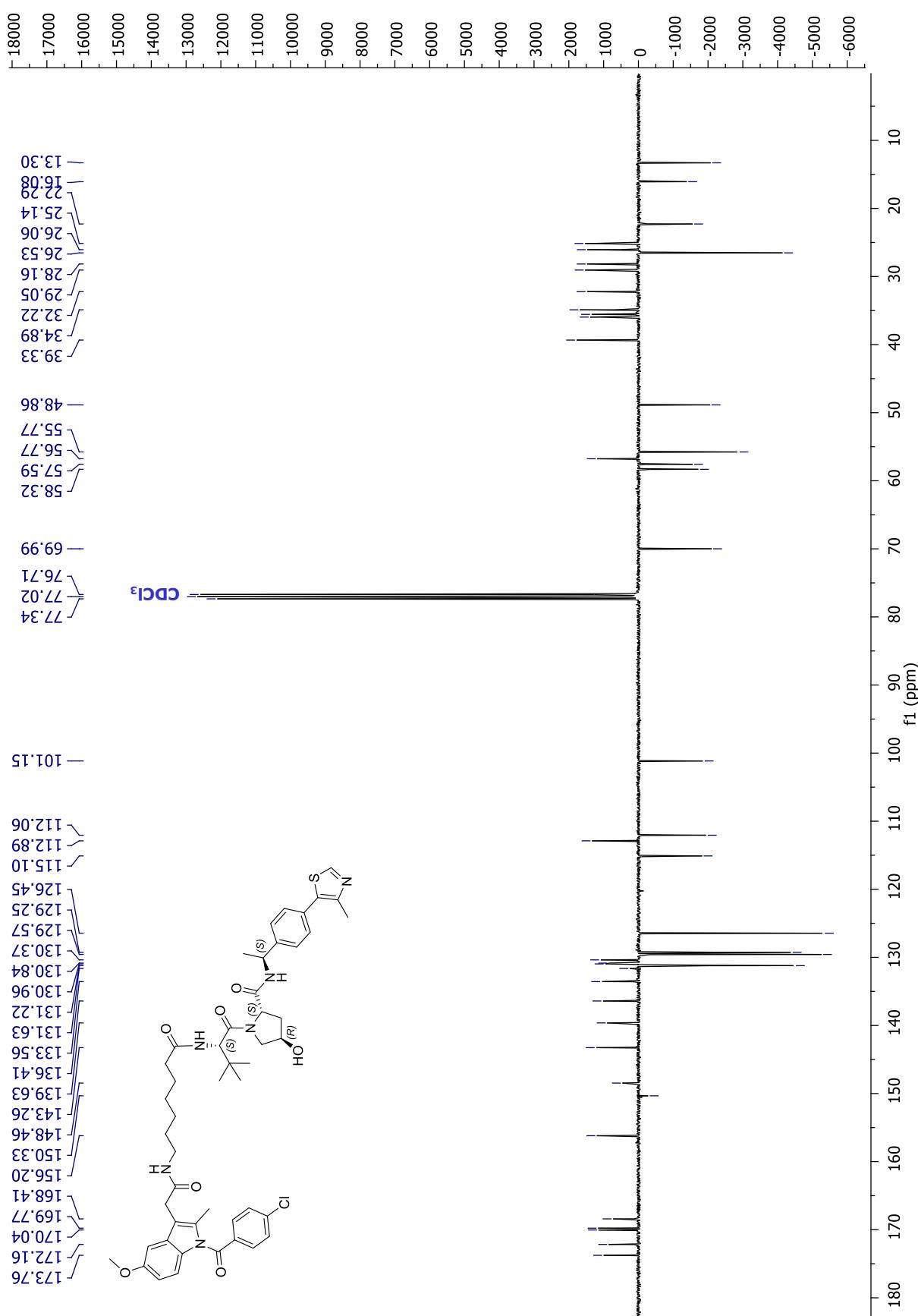


Figure S6. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 3.

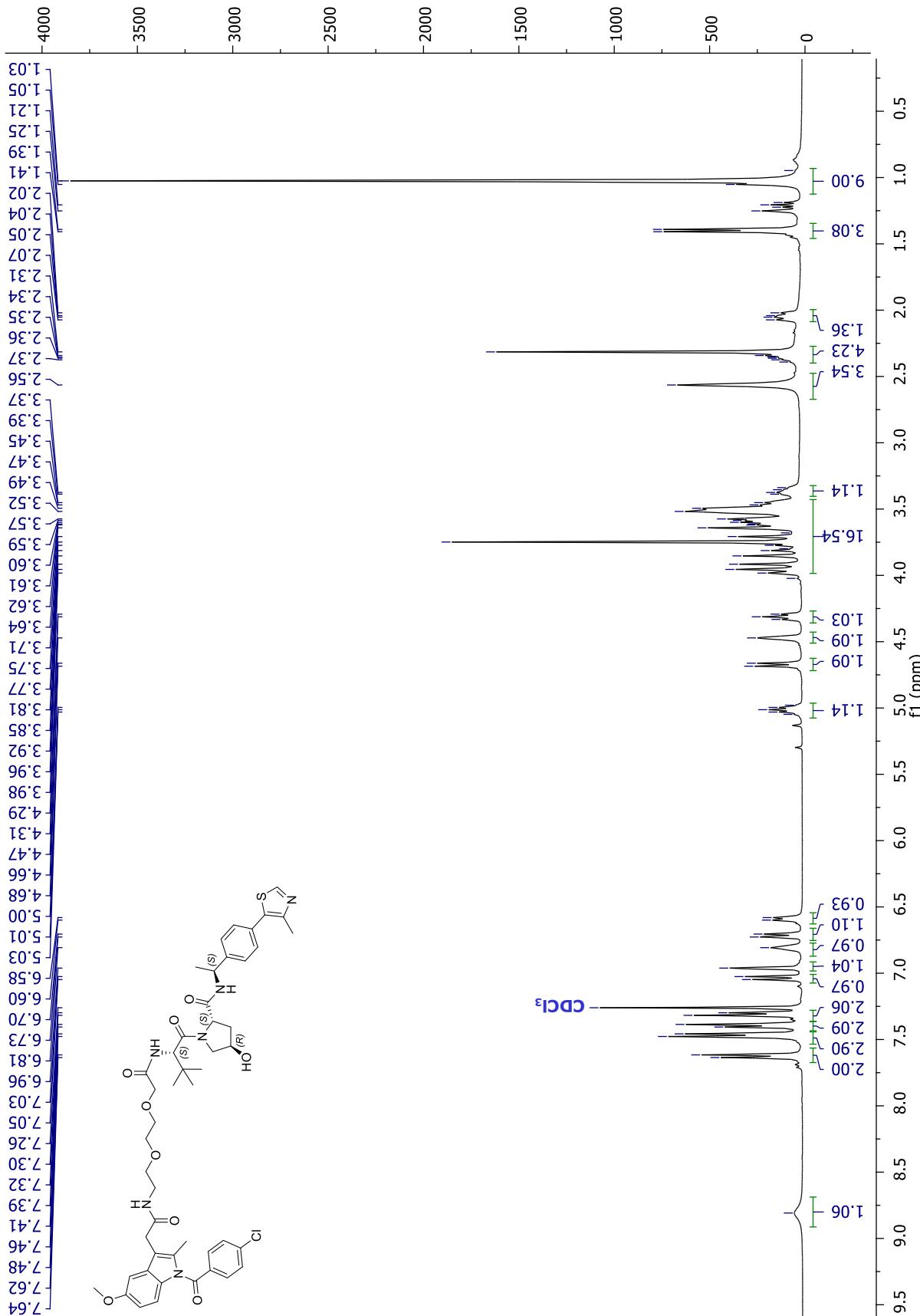


Figure S7. ^1H NMR (400 MHz, CDCl_3) spectrum of compound 4.

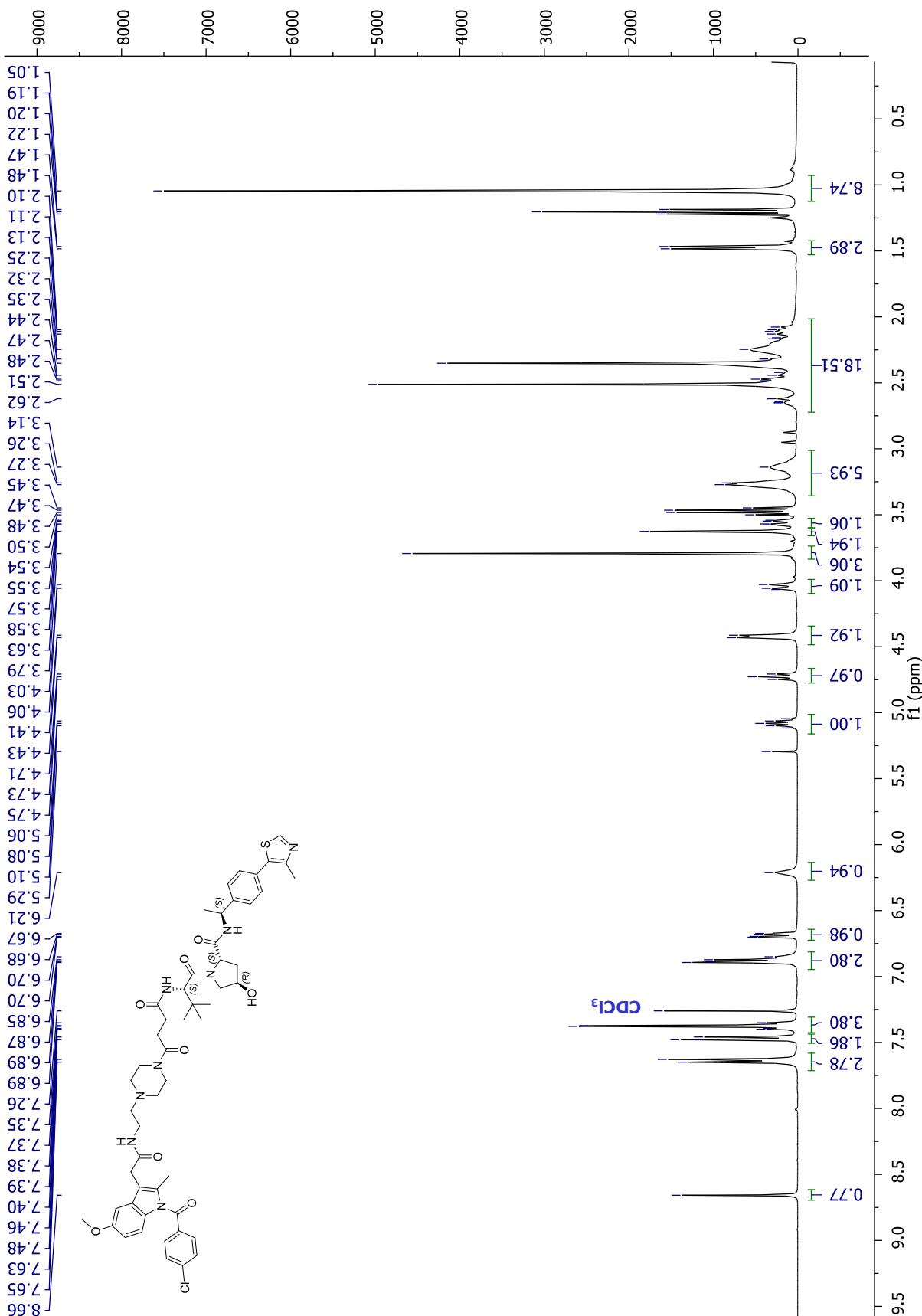


Figure S8. ^1H NMR (400 MHz, CDCl_3) spectrum of compound 5.

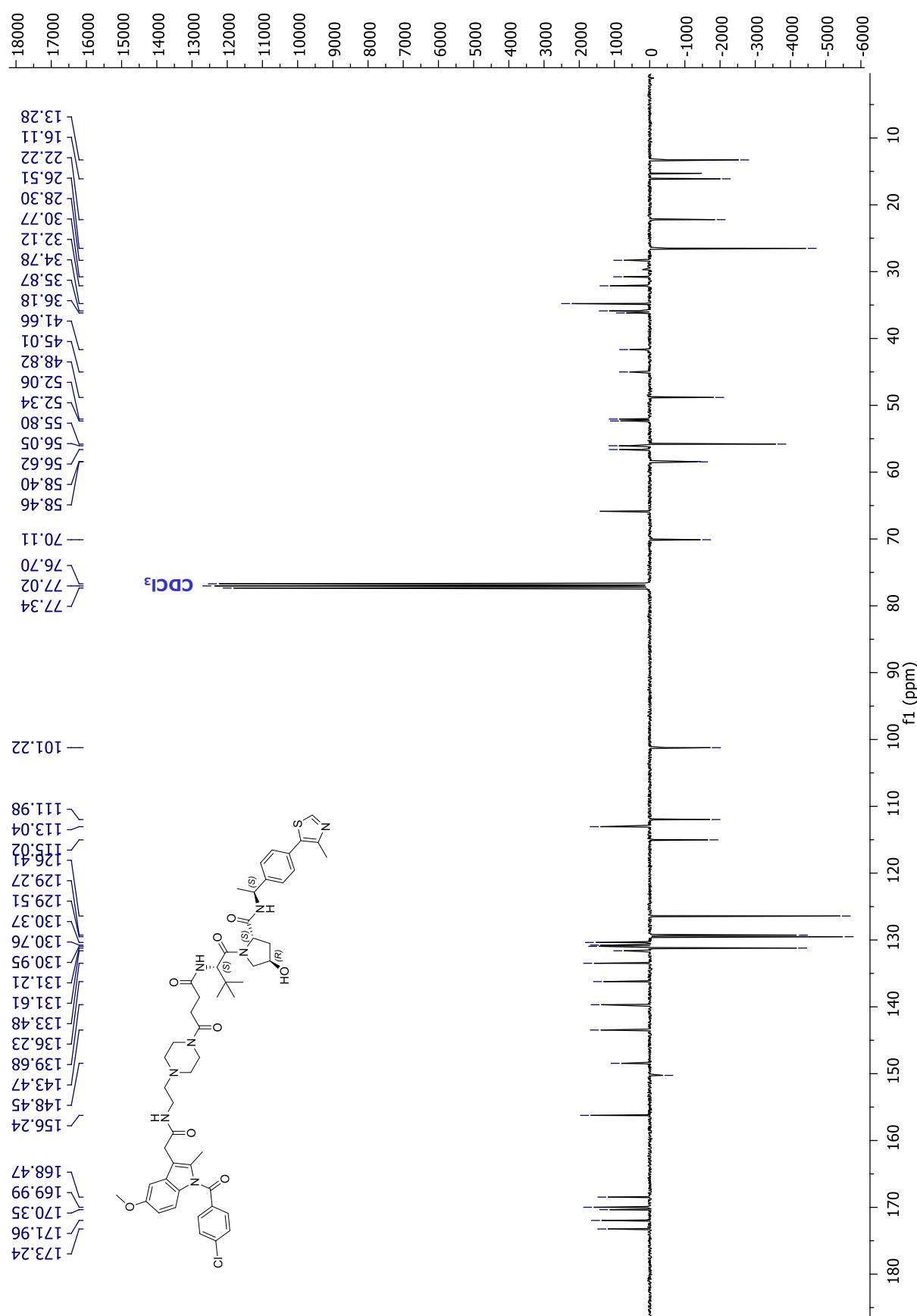


Figure S9. ¹³C NMR (101 MHz, CDCl₃) spectrum of compound 5.

Table S1

Compound	NMR Chemical Shift
2	<p>¹H NMR (400 MHz, CDCl₃) δ 8.72 (s, 1H), 7.66 (d, <i>J</i> = 8.3 Hz, 2H), 7.47 (d, <i>J</i> = 8.3 Hz, 2H), 7.44-7.28 (m, 5H), 6.97 (d, <i>J</i> = 2.3 Hz, 1H), 6.91 (d, <i>J</i> = 9.0 Hz, 1H), 6.69 (dd, <i>J</i> = 8.9, 2.3 Hz, 1H), 6.34 (d, <i>J</i> = 8.8 Hz, 1H), 5.92 (t, <i>J</i> = 5.9 Hz, 1H), 5.13-5.02 (m, 1H), 4.73 (t, <i>J</i> = 8.0 Hz, 1H), 4.51 (d, <i>J</i> = 8.9 Hz, 1H), 4.46 (s, 1H), 4.02 (d, <i>J</i> = 11.7 Hz, 1H), 3.80 (s, 3H), 3.72-3.57 (m, 2H), 3.53 (dd, <i>J</i> = 11.3, 3.3 Hz, 1H), 3.32-3.19 (m, 1H), 3.14-3.00 (m, 1H), 2.62-2.46 (m, 4H), 2.36 (s, 3H), 2.20 (t, <i>J</i> = 6.7 Hz, 2H), 2.12-2.00 (m, 1H), 1.61-1.50 (m, 2H), 1.49-1.35 (m, 5H), 1.01 (s, 9H).</p> <p>¹³C NMR (101 MHz, CDCl₃) δ 173.43, 172.18, 170.40, 169.69, 168.53, 156.27, 150.45, 147.77, 143.47, 139.59, 136.54, 133.61, 131.29, 131.18 (2C), 130.99, 130.48, 130.38, 129.54 (2C), 129.24 (2C), 126.51 (2C), 115.11, 112.86, 112.11, 101.26, 70.00, 58.35, 57.52, 56.89, 55.84, 48.86, 38.52, 35.39, 35.18, 35.11, 32.09, 28.47, 26.49 (3C), 22.25, 21.87, 15.79, 13.40.</p>
3	<p>¹H NMR (400 MHz, CDCl₃) δ 8.67 (s, 1H), 7.66 (d, <i>J</i> = 8.3 Hz, 2H), 7.52 (d, <i>J</i> = 8.0 Hz, 1H), 7.48 (d, <i>J</i> = 8.2 Hz, 2H), 7.44-7.34 (m, 4H), 6.93 (d, <i>J</i> = 2.4 Hz, 1H), 6.87 (d, <i>J</i> = 9.1 Hz, 1H), 6.69 (dd, <i>J</i> = 9.2, 2.0 Hz, 1H), 6.27 (d, <i>J</i> = 8.3 Hz, 1H), 5.77-5.68 (m, 1H), 5.14-5.03 (m, 1H), 4.74 (t, <i>J</i> = 7.9 Hz, 1H), 4.57 (d, <i>J</i> = 8.6 Hz, 1H), 4.47 (s, 1H), 4.13 (d, <i>J</i> = 11.7 Hz, 1H), 3.82 (s, 3H), 3.62 (s, 2H), 3.57 (dd, <i>J</i> = 11.4, 3.2 Hz, 1H), 3.16 (dd, <i>J</i> = 13.5, 7.1 Hz, 2H), 2.59-2.43 (m, 4H), 2.37 (s, 3H), 2.26-2.02 (m, 3H), 1.65-1.44 (m, 5H), 1.44-1.29 (m, 2H), 1.30-1.14 (m, 4H), 1.04 (s, 9H).</p> <p>¹³C NMR (101 MHz, CDCl₃) δ 173.76, 172.16, 170.04, 169.77, 168.41, 156.20, 150.33, 148.46, 143.26, 139.63, 136.41, 133.56, 131.63, 131.22 (2C), 130.96, 130.84, 130.37, 129.57 (2C), 129.25 (2C), 126.45 (2C), 115.10, 112.89, 112.06, 101.15, 69.99, 58.32, 57.59, 56.77, 55.77, 48.86, 39.33, 35.96, 35.56, 34.89, 32.22, 29.05, 28.16, 26.53 (3C), 26.06, 25.14, 22.29, 16.08, 13.30.</p>
4	<p>¹H NMR (400 MHz, CDCl₃) δ 8.81 (s, 1H), 7.63 (d, <i>J</i> = 8.0 Hz, 2H), 7.47 (d, <i>J</i> = 7.9 Hz, 3H), 7.40 (d, <i>J</i> = 7.9 Hz, 2H), 7.31 (d, <i>J</i> = 7.8 Hz, 2H), 7.04 (d, <i>J</i> = 9.0 Hz, 1H), 6.96 (s, 1H), 6.81 (s, 1H), 6.72 (d, <i>J</i> = 8.8 Hz, 1H), 6.59 (d, <i>J</i> = 7.7 Hz, 1H), 5.08-4.96 (m, 1H), 4.67 (d, <i>J</i> = 9.2 Hz, 1H), 4.47 (s, 1H), 4.31 (t, <i>J</i> = 7.9 Hz, 1H), 3.99-3.43 (m, 16H), 3.40-3.32 (m, 1H), 2.56 (s, 3H), 2.40-2.27 (m, 4H), 2.09-2.00 (m, 1H), 1.40 (d, <i>J</i> = 6.8 Hz, 3H), 1.01 (s, 9H).</p>
5	<p>¹H NMR (400 MHz, CDCl₃) δ 8.66 (s, 1H), 7.64 (d, <i>J</i> = 8.4 Hz, 3H), 7.47 (d, <i>J</i> = 8.5 Hz, 2H), 7.43-7.31 (m, 4H), 6.88 (dd, <i>J</i> = 11.5, 5.9 Hz, 3H), 6.69 (dd, <i>J</i> = 9.1, 2.3 Hz, 1H), 6.21 (s, 1H), 5.16-5.01 (m, 1H), 4.73 (t, <i>J</i> = 8.3 Hz, 1H), 4.49-4.34 (m, 2H), 4.10-3.99 (m, 1H), 3.82 (s, 3H), 3.63 (s, 2H), 3.56 (dd, <i>J</i> = 11.3, 2.7 Hz, 1H), 3.36-3.01 (m, 6H), 2.70-2.06 (m, 18H), 1.48 (d, <i>J</i> = 6.9 Hz, 3H), 1.05 (s, 9H).</p> <p>¹³C NMR (101 MHz, CDCl₃) δ 173.24, 171.96, 170.35, 169.99 (2C), 168.47, 156.24, 150.26, 148.45, 143.47, 139.68, 136.23, 133.48, 131.61, 131.21 (2C), 130.95, 130.76, 130.37, 129.51 (2C), 129.27 (2C), 126.41 (2C), 115.02, 113.04, 111.98, 101.22, 77.34, 77.02, 76.70, 70.11, 58.46, 58.40, 56.62, 56.05, 55.80, 52.34, 52.06, 48.82, 45.01, 41.66, 36.18, 35.87, 34.78, 32.12, 30.77, 28.30, 26.51 (3C), 22.22, 16.11, 13.28.</p>
10	<p>¹H NMR (400 MHz, MeOD) δ 3.62 – 3.55 (m, 4H), 3.21 (t, <i>J</i> = 6.6 Hz, 2H), 2.68 – 2.63 (m, 2H), 2.61 – 2.54 (m, 4H), 2.54 – 2.47 (m, 4H), 1.44 (s, 9H).</p>

14	¹H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 8.98 (s, 1H), 8.37 (d, <i>J</i> = 7.8 Hz, 1H), 7.86 (d, <i>J</i> = 9.2 Hz, 1H), 7.47 – 7.34 (m, 4H), 6.78 (s, 1H), 5.09 (d, <i>J</i> = 3.0 Hz, 1H), 4.92 (dd, <i>J</i> = 14.0, 6.8 Hz, 1H), 4.49 (d, <i>J</i> = 9.3 Hz, 1H), 4.42 (t, <i>J</i> = 8.1 Hz, 1H), 4.28 (s, 1H), 3.65 – 3.40 (m, 5H), 3.32 (s, 3H), 3.20 – 3.06 (m, 3H), 2.45 (s, 4H), 2.42 – 2.26 (m, 2H), 2.05 – 1.96 (m, 1H), 1.85 – 1.74 (m, 1H), 1.48 – 1.28 (m, 12H), 1.28 – 1.19 (m, 1H), 0.93 (s, 9H).
18	¹H NMR (400 MHz, DMSO- <i>d</i> ₆) δ 8.99 (s, 1H), 8.39 (d, <i>J</i> = 7.8 Hz, 1H), 8.25 (bs, 3H), 7.89 (d, <i>J</i> = 8.9 Hz, 1H), 7.43 (d, <i>J</i> = 8.2 Hz, 2H), 7.38 (d, <i>J</i> = 8.3 Hz, 2H), 4.95 – 4.88 (m, 1H), 4.50 (d, <i>J</i> = 9.4 Hz, 1H), 4.42 (t, <i>J</i> = 8.3 Hz, 1H), 4.28 (s, 1H), 3.64 – 3.53 (m, <i>J</i> = 16.0 Hz, 11H), 2.65 – 2.54 (m, <i>J</i> = 10.2 Hz, 4H), 2.45 (s, 3H), 2.07 – 1.96 (m, <i>J</i> = 9.7 Hz, 1H), 1.83 – 1.73 (m, 1H), 1.37 (d, <i>J</i> = 6.9 Hz, 3H), 1.30 – 1.21 (m, 1H), 0.94 (s, 9H).